



# Operation: Present and Future

<http://protein.nsls.bnl.gov>





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## Mission

The East Coast NIGMS Structural Biology Facility mission is to provide first class resources to the biological- biochemical-, and biophysics- communities to explore all aspects of structural biology. It is the goal of this facility to provide assistance to expert and non-expert crystallographers.

These goals include:

- Beam line access to a structural biology community at large.
- Fast access to beam time for the user community.
- Crystal screening and high-throughput data collection.
- Assistance and training for academic and professional users.

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# Background





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## NIGMS Initiative in 1999\*

- Beamline upgrades for benefit of general users
- Reports on increasing demand for user access and beamline needs
- Estimate of doubling of capacity for crystallographic experiments from staff increases and equipment upgrades
- Letter to synchrotron facility directors inviting informal proposals
- NIGMS synchrotron advisory group
- FY99 funding of \$7M from NIGMS

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\* source Norvell, Aug1999





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## The NIGMS support at the NSLS

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- construction of bending magnet beamline
- including beamline optics, monochromator, detector, crystallography station
- four beamline scientists/technicians
- \$2,372K equipment/construction
- \$670K annual – staff and operation

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# Facility Resources



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# Optics

Optical element					
	<i>crystal channel cut</i>	<i>energy range</i>	<i>band pass</i>	<i>Intensity</i>	<i>spot size</i>
monochromator	Si(111)	6 -23 keV	$1.9 \times 10^{-4}$	$1.2 \times 10^{10}$ ph/s	$0.1 \times 0.5 \text{ mm}^2$
	coating	figure	magnification	acceptance	
mirror	Rh	Thoroidal	1:1	3mrad	

\* I=230 mA, 200 $\mu$ m slits at 1.2 Å

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# Experimental Control



<i>Beam Line</i>	EPICS/VME
<i>Diffractometer</i>	Compumotors
<i>Goniometer</i>	Galil
<i>Automounter</i>	Wago
<i>In line sample viewer</i>	Wago



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# Computer Infrastructure

Experiment control	1TB RAID 10 system, Dual AMD Opteron 242 Dual Gigabit network
Data Analysis	twin RAID 10 system
Data Analysis - Firewall	130GB SCSI Dual Athlon MP
Backup - Long Term Storage; Data Analysis:	1TB RAID 5 system, Dual AMD Opteron 248 Dual Gigabit network

Data Collection	BluIce/DCS
Data Processing	HKL2000, MOSFLM
Data Analysis and Refinement	ShelX, CCP4, SOLVE, RESOLVE, CNS,etc
Model Building	Coot, O



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## Lab Facilities

### X6A User support:

- Crystallization
- Sample handling
- Cryogenics

### NSLS User support:

- Chemistry
- Wet Lab
- Sample Handling



### Equipment

- ❖ Akta Explorer 10 for purification
- ❖ Centrifuges
- ❖ UV spectrometer
- ❖ Fast Gel-system
- ❖ Incubators for controlled temperature crystallization
- ❖ pH meters, balances





# Technical Upgrades and Developments





# Hardware

## Upgrade

- Detector power supply and optical cables
- Computer workstations

## Development

- Automounter Lid - NSLS
- Automounter Liquid Nitrogen Supply - NSLS
- Sample in line viewer - NSLS



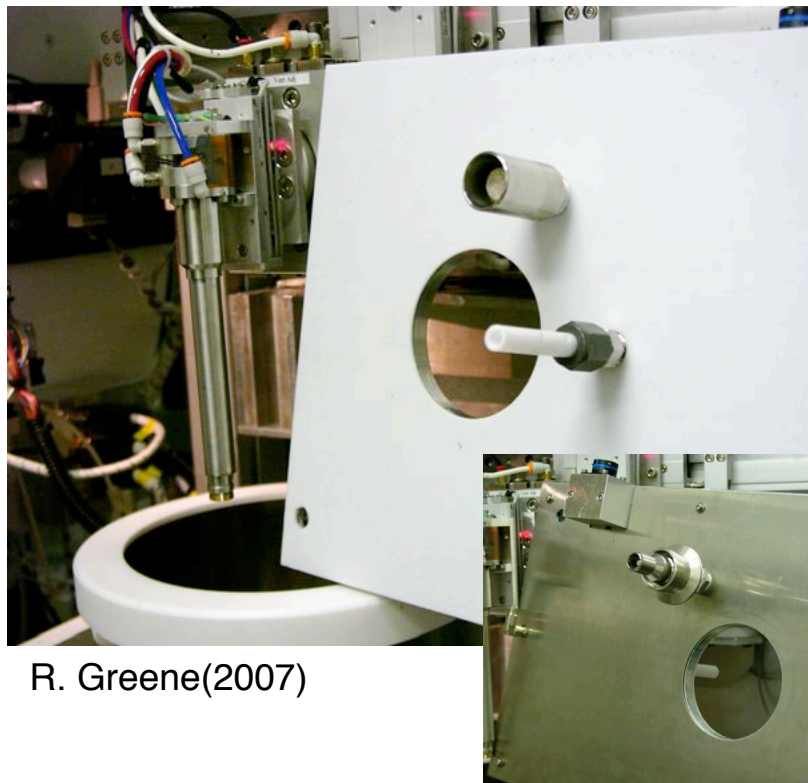
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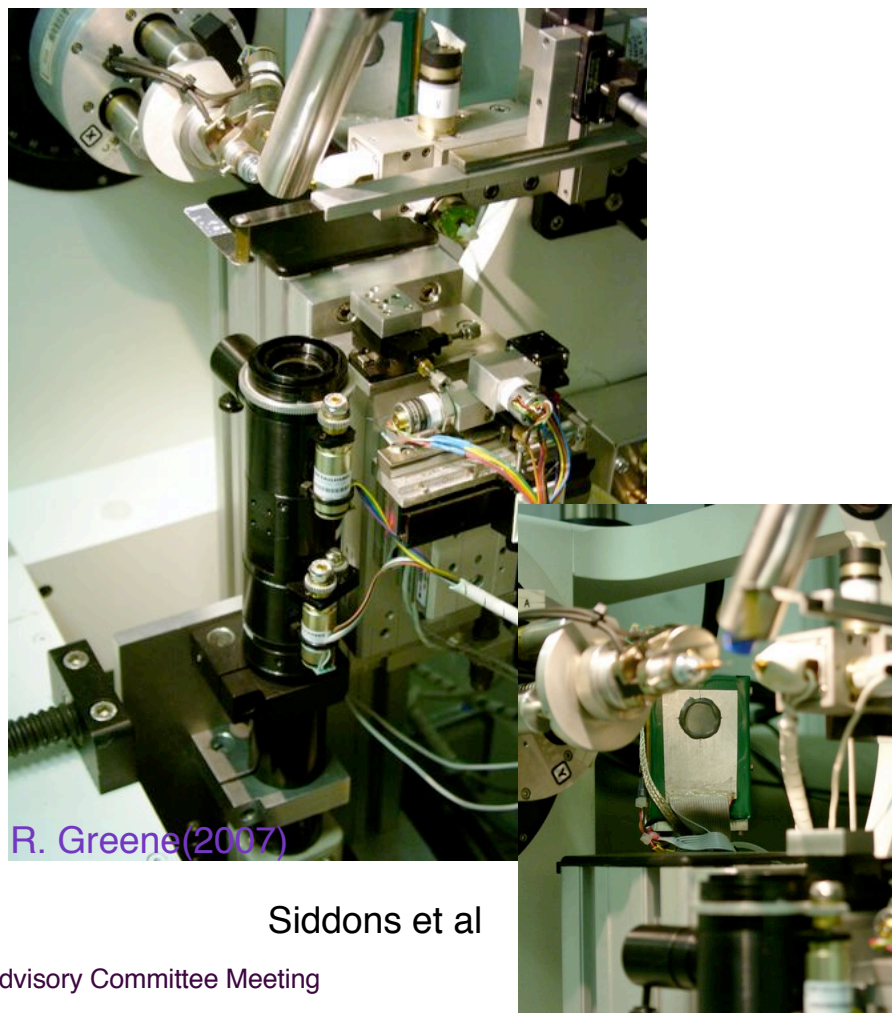
# Hardware

New Automounter dewar lid



R. Greene(2007)

Sample in line viewer and  
Fluorescence detector



R. Greene(2007)

Siddons et al

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# Hardware

Planned Upgrade (time line 31 July 2008)

## ➤ Diffractometer - Crystallogic

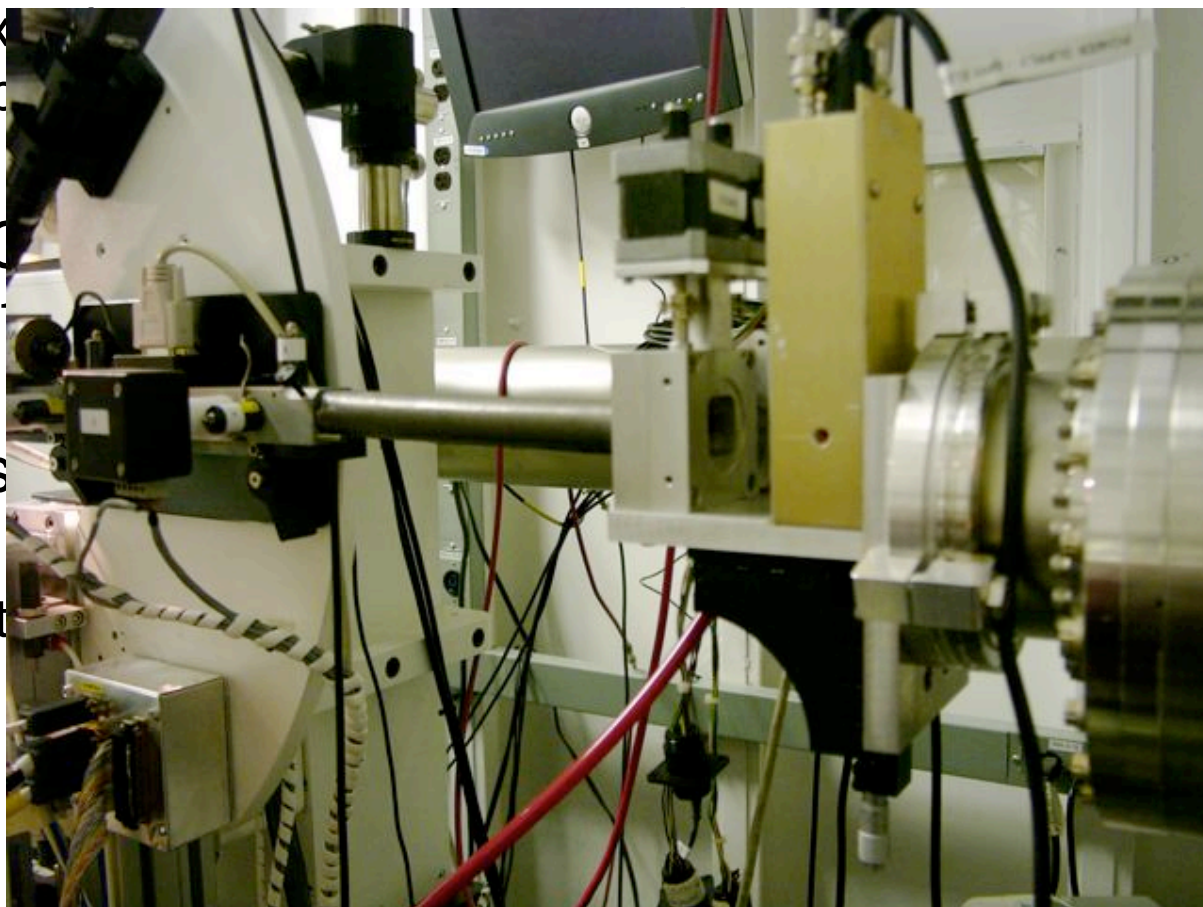
- ❖ Rotation axis
- ❖ Slit assembly

## ➤ Detector - ADSC

- ❖ From a Q2

## ➤ Upstream slit as

- ❖ Secondary
- ❖ Beam posit



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# Software

## Upgrade

Smaller implementations

- Blulce / DCS
- Computer workstations

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## Development

- Crysis

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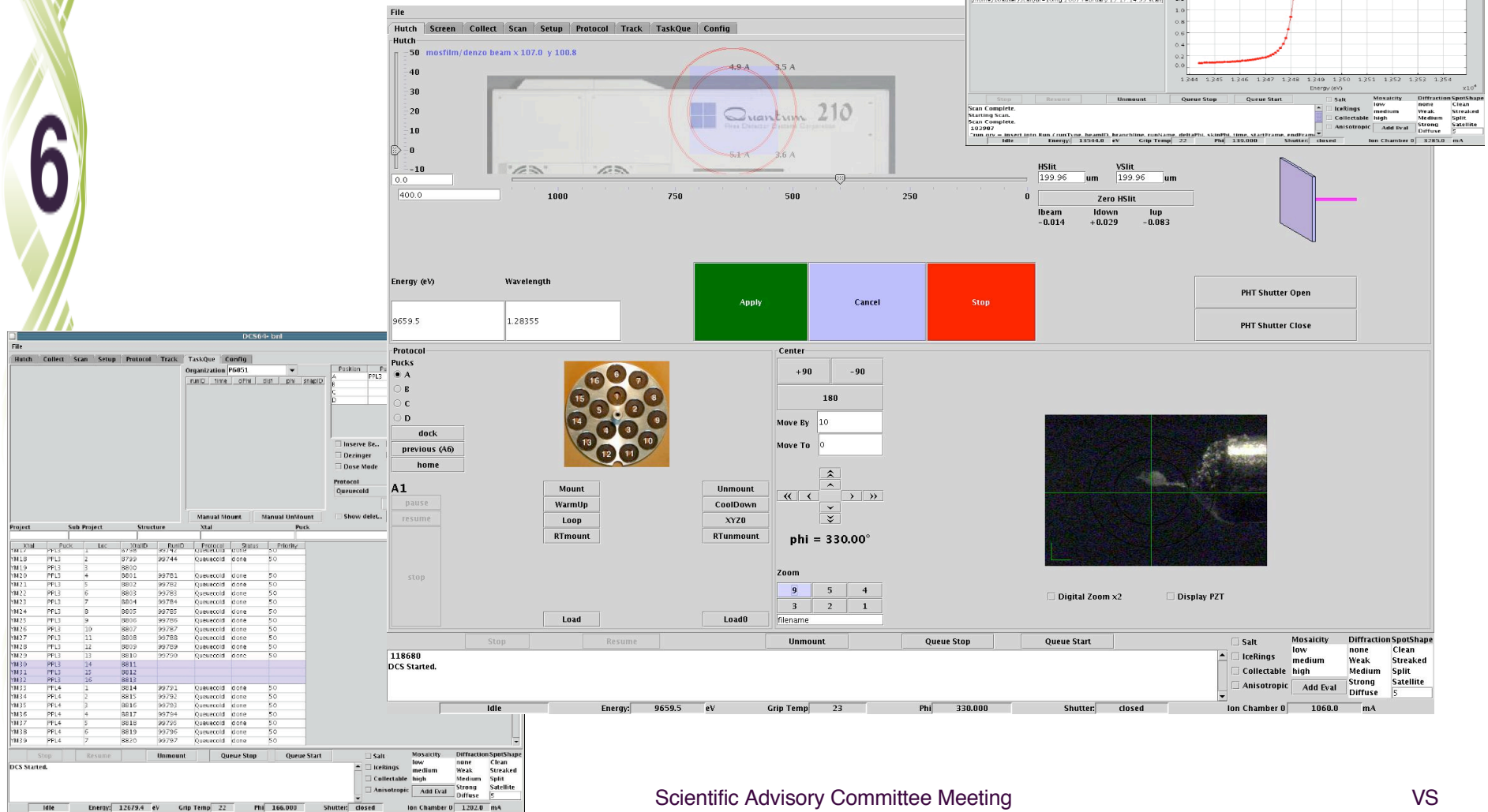


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Blulce/DCS

Need to be Beam Line Specific!

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# CrysCent

CryCent (Crystal Centering) is a software designed to center protein crystals without human interference.

Follows a “human” Protocol

- Uses machine vision and image processing techniques
- Is Platform-independent
- Zero-click, fully automatic crystal centering



Current Status:

- Operational

Problems:

- hardware is not stable enough

Anubhav Jain, Cornell University SULI Program, DOE





# X Crysis

CrySis (Crystal Analysis) is a software designed to serve as an automated quality control tool for protein crystallography diffraction patterns.

## 6 CrySis

- Is based on Neural Network algorithms.
- Uses machine vision and image processing techniques
- Is Platform-independent
- Allows for automated crystal and diffraction quality assessment.

Alec Berntson, Cornell University SULI Program, DOE

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# X Crysis

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*Under commissioning*

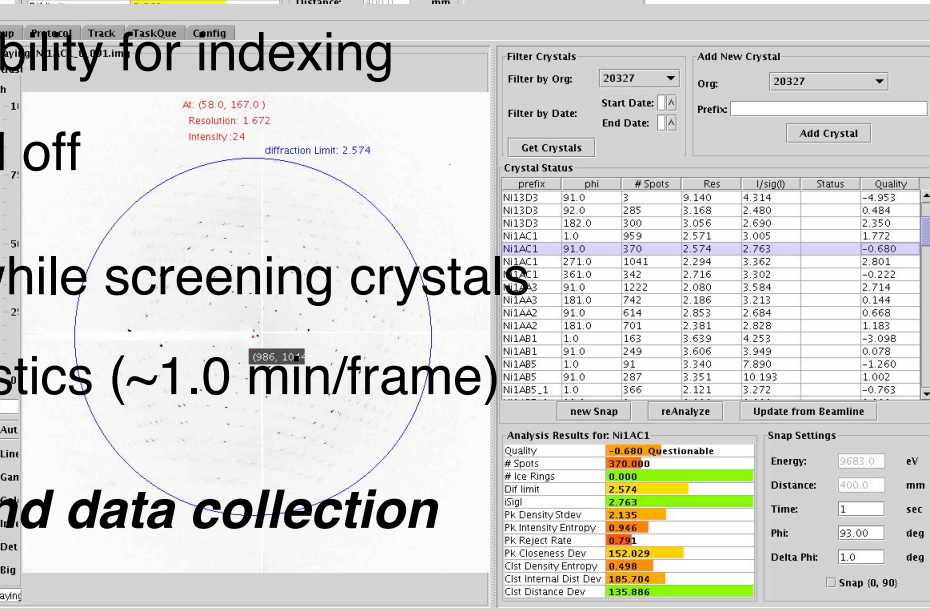
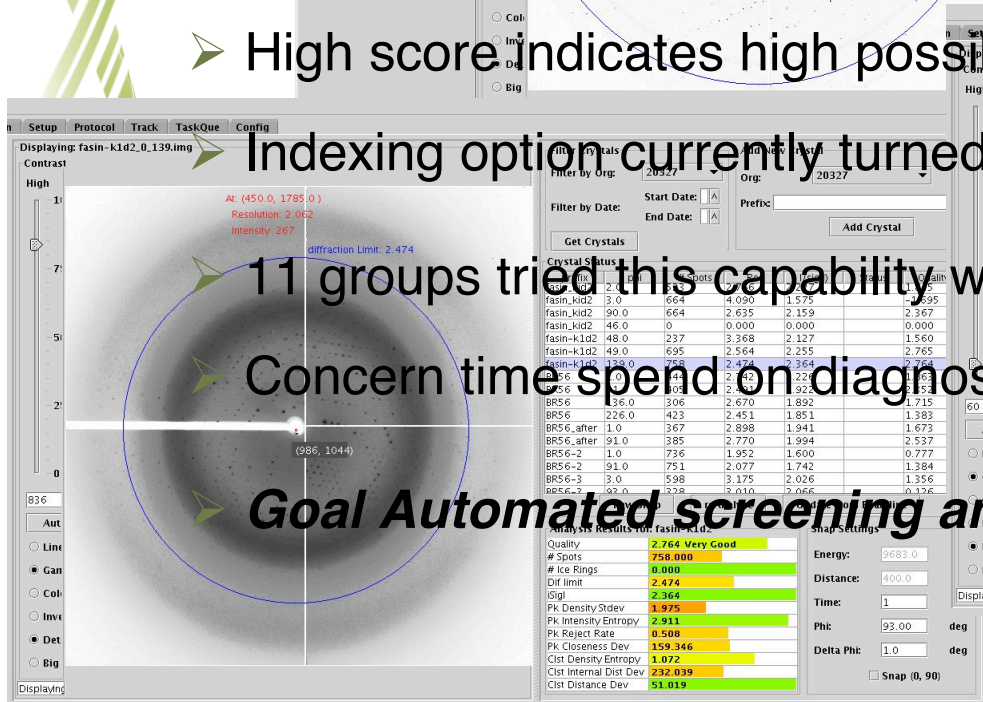
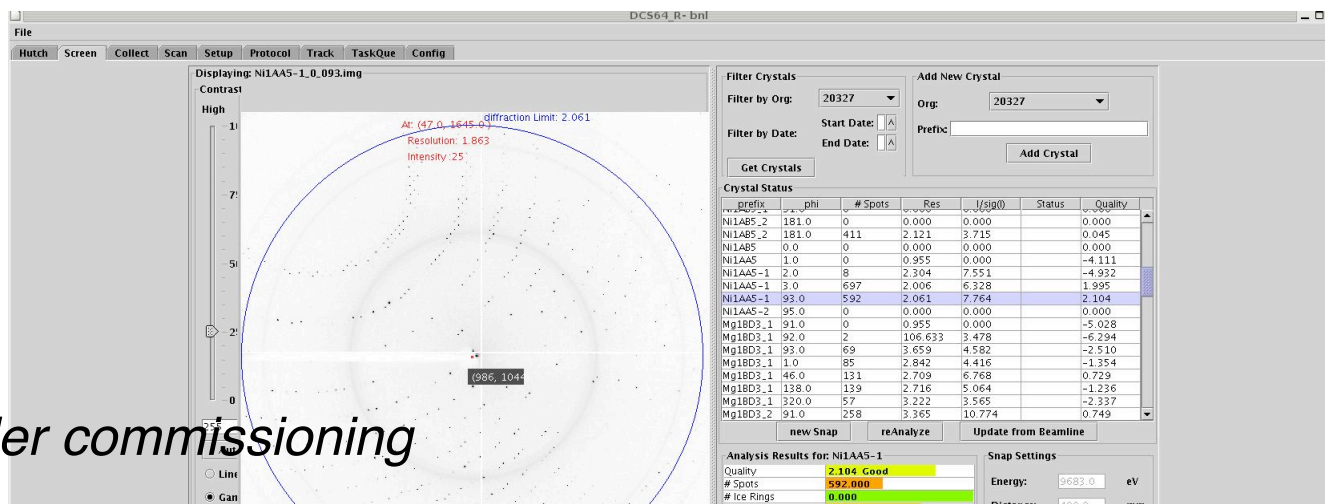
- High score indicates high possibility for indexing

- Indexing option currently turned off

- 11 groups tried this capability while screening crystals

- Concern time spend on diagnostics (~1.0 min/frame)

- **Goal Automated screening and data collection**



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# Software

Planned Upgrade (time line 31 July 2008)

- Computer workstations
- Install a small Laptop inside the hutch to control the automounter and allow goniohead centering
- Integrate further CrysCent and CrysSis to allow for fully automated sample screening



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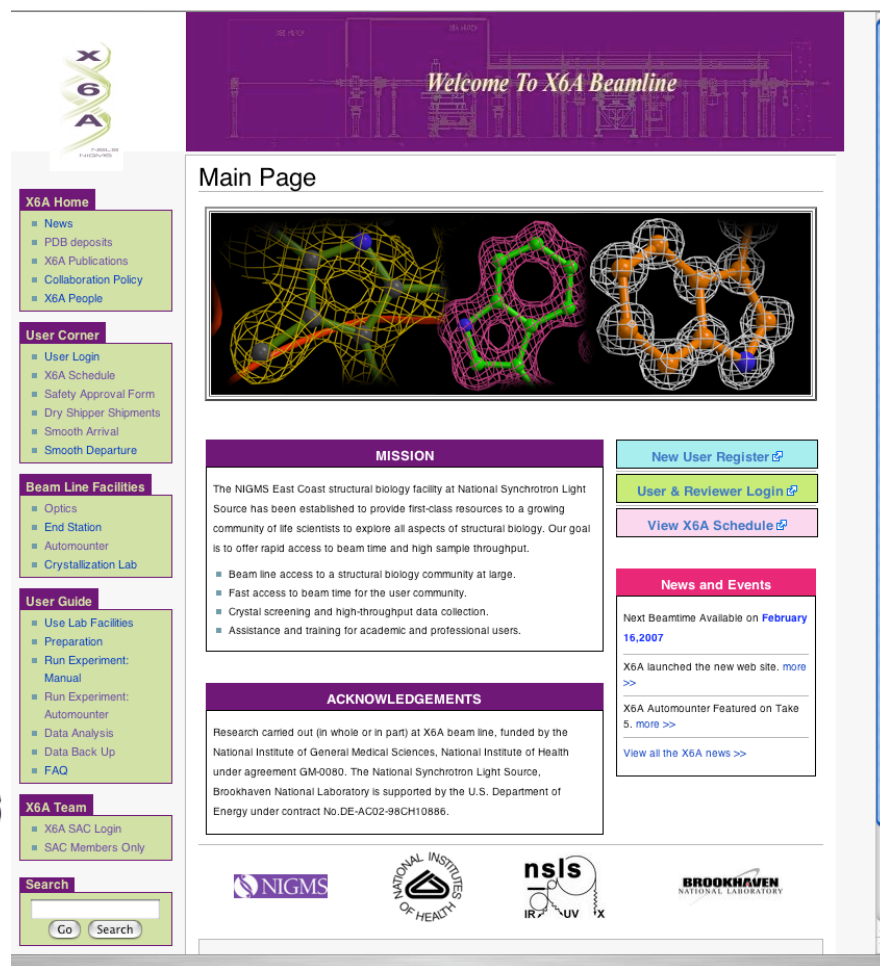
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# The X6A Web and Data Base Environment

Re-Designed last year has as purpose



Media Wiki

➤ Improve communication

User and Experimental Control  
Databases

➤ Communication between  
databases

User Database

➤ Improve User Access  
➤ Improve Beam Line Management  
➤ Real time Statistical Analysis of  
beam time usage

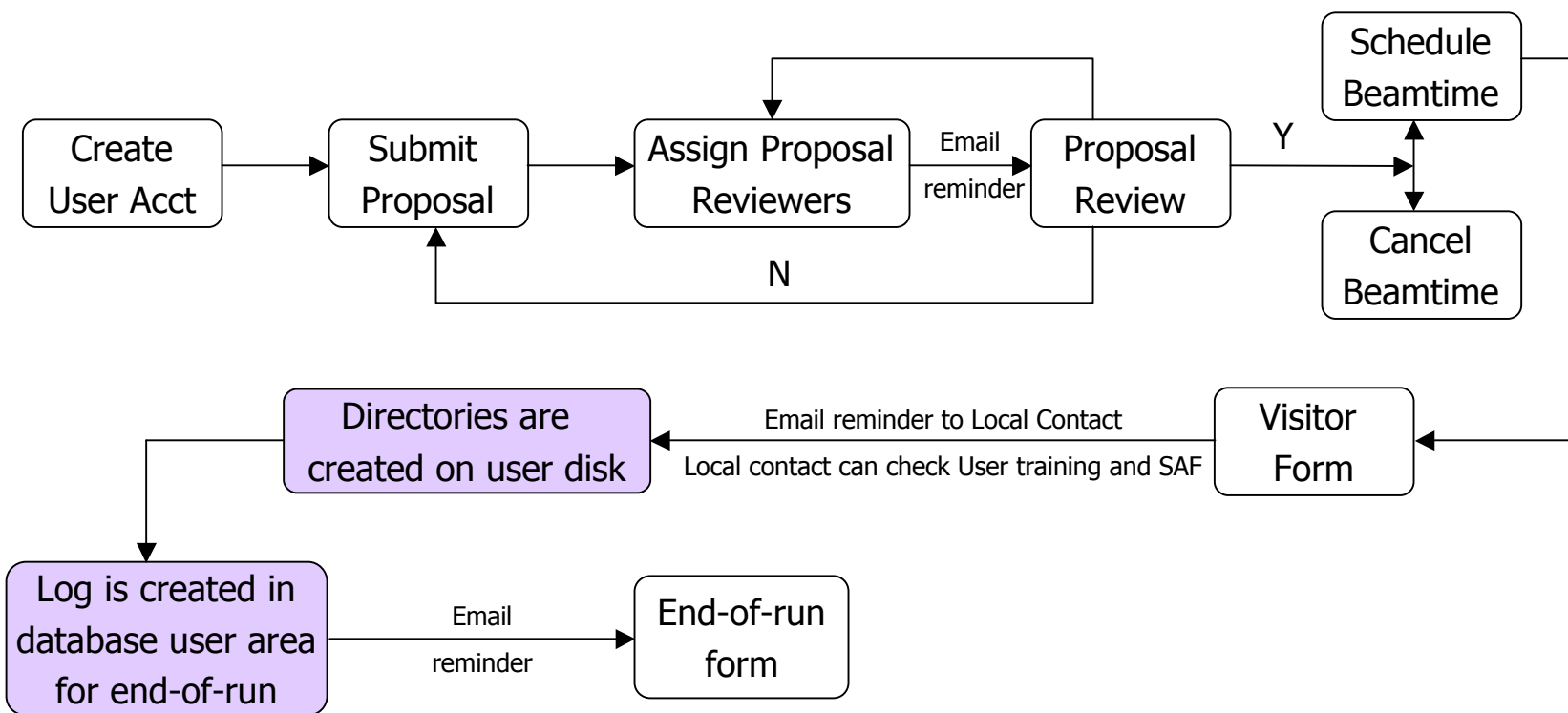


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# The X6A Web and Data Base Environment



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# The X6A Web and Data Base Environment

## User Database

### ➤ Improve User Access

My Account

Edit User Profile  
Change Password  
Build Collaborator List  
LOG OUT  
Account Status

## User -> Account Status

Welcome, AMOR

### Schedule Status

#### Current or Future Schedules

You have 0 schedule(s)

### Projects Status

#### Incomplete Projects

You have 0 Incomplete Project(s)

#### Choose Projects for Schedule

Currently You have 1 projects ready for scheduling  
Select AS MANY PROJECTS AS YOU WANT to schedule your beamtime for these projects.

Project No.	Proposal Title	Submitted Date	select
x6a1	High resolution studies of a thermostable xylanase	2002-10-07	<input checked="" type="checkbox"/>

## X6A STAFF -> User Experiment Follow Up

Schedule

Prev <<

Visit Status: Pending

Mark Start Time 2007-02-16 12:00:00 Mark End Time 2007-02-19 12:00:00

### Experiment Overview [ + More Details ]

crystal	filePath	createDate	images
4d3-1	/data_cys/User/X6969/2007-02-16/Collect/4d3-1	2007-02-17 23:09:55	120
4d3-1	/data_cys/User/X6969/2007-02-16/Screen	2007-02-17 21:56:40	4
4c4-3	/data_cys/User/X6969/2007-02-16/Collect/4c4-3	2007-02-17 20:42:07	120
4c4-3	/data_cys/User/X6969/2007-02-16/Screen	2007-02-17 18:28:04	3
4c4-2	/data_cys/User/X6969/2007-02-16/Screen	2007-02-17 18:15:20	2
4c4-1	/data_cys/User/X6969/2007-02-16/Collect/4c4-1	2007-02-17 16:53:17	180
4c4-1	/data_cys/User/X6969/2007-02-16/Screen	2007-02-17 14:33:01	5
1b4-1	/data_cys/User/X6969/2007-02-16/Collect/1b4-1	2007-02-17 13:05:46	180

### Available Beamtime Slots:

From	To	Duration
2007-02-19 12:00:00 (Monday)	2007-02-19 20:00:00 (Monday)	8days 8hours
2007-02-27 08:00:00 (Tuesday)	2007-02-27 12:00:00 (Tuesday)	4hours
2007-03-04 00:00:00 (Sunday)	2007-03-05 06:00:00 (Monday)	1days 6hours
2007-03-06 12:00:00 (Tuesday)	2007-03-12 12:00:00 (Monday)	6days 0hours

4 MA: x6a85 Maintenance [From: 06:00:00 To: 11:59:59] NSLS Studies [From: 12:00:00 To: 11:59:59] x6a121 NSLS Studies [From: 12:00:00 To: 11:59:59] x6a180 NSLS Studies [From: 12:00:00 To: 11:59:59]

11 MA: x6a178 USER Available [From: 12:00:00 To: 11:59:59] x6a176 NSLS Studies [From: 12:00:00 To: 11:59:59] x6a172 NSLS Studies [From: 12:00:00 To: 11:59:59]

18 JJ: x6a173 USER Available [From: 12:00:00 To: 11:59:59] x6a181 NSLS Studies [From: 12:00:00 To: 11:59:59] x6a172 NSLS Studies [From: 12:00:00 To: 11:59:59]

25 JJ: x6a173 USER Available [From: 12:00:00 To: 11:59:59] x6a181 NSLS Studies [From: 12:00:00 To: 11:59:59] x6a172 NSLS Studies [From: 12:00:00 To: 11:59:59]

### Manage Projects

- Create new proposals
- Create new proposals based on existing projects
- Edit proposals
- View projects
- Assign project members
- Find review results

### Manage Schedule

- View X6A Schedules
- Create new schedules

### Visit (Experiment) Information

Fields marked with \* are required.

Visitors \*

Experimenters who will actually visit the beamline (Press Ctrl Key to achieve multiple choices)

Stojanoff Vivian  
Olivier Nelson  
No visitors

(The name not shown in the List? Build Collaborator List now.)

Sample Safety

Do your samples have hazards \*

☐ Biological hazards ☐ Any Risks ☐ No Hazard ☐ Uncertain

If any hazards or risks, give details of possible hazards

Sample Shipment (ship your sample to x6a)

Date user shipped Format: YYYY-MM-DD Shipment Type Tracking Number Date X6A staff received Format: YYYY-MM-DD

Sample Back Shipment (ship your sample back)

Date X6A staff shipped Format: YYYY-MM-DD Shipment Type Tracking Number Date you received Format: YYYY-MM-DD

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Statistic

BeamTime Analysis  
Local Contact Analysis  
Reviewer Analysis  
User Analysis  
Survey Analysis

Assignment

Assign/Edit Local Contact  
Assign User Level  
Assign Reviewer Status  
Assign New Reviewers

Miscellaneous

Admin Duty  
Create X6A schedules  
Delete X6A schedules  
Add projects to Visits  
User Shipments



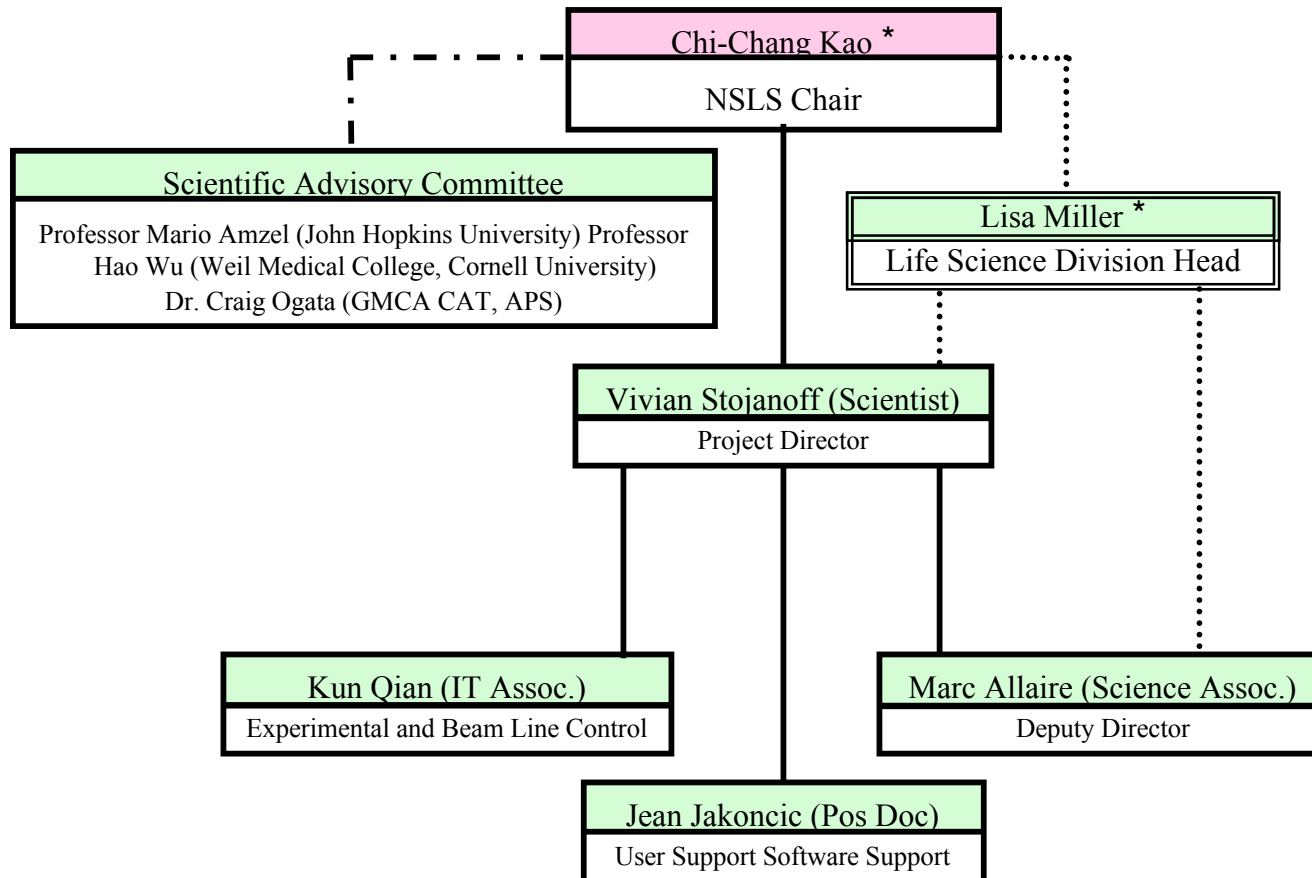


# Staff





# Organizational Chart



\* NSLS scientific staff





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# NSLS staff contributing to the operation

## Technical support provide by the NSLS as needed

Peter Siddons	Detectors
(T. Kuczewski)	
Steve Hulbert	Beamline Support
(S. Cheung, R. Greene, T. Lenhard)	
Z. Yin	Computer & Control
Wayne Rambo	Electrical Support
(B. Clay, D. Poshka)	

## Administrative support provide by the NSLS as needed

Brian Boyle	Budget Administration
(W. Morrin)	
Eileen Morello	Secretarial Support
(A. Bowden)	
Katheleen Nasters	User Administration
(G. Cisco, L. Flynn, M. Baez)	
A. Ackerman	EH&S
(J. Aloï)	
B. Kiss	Building Management





# User Program

*aaahhhh...personal attention! I love it!*  
*CM*





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# User access

Two modes are available to users for beam time application:

- X6A Fast Access (<http://protein.nsls.bnl.gov>)
  - ❖ Projects submitted through the X6A application form
  - ❖ Single Projects (1Protein = 1Project)
  - ❖ Easy, simple and fast (3 days to a week review process)
  - ❖ Multiple visits
  - ❖ User schedules own beam time
- General User proposals submitted through the PASS system
  - ❖ Two modes of application:
    - ✓ general users beam time: 4 month in advance valid for
    - ✓ rapid access (valid for current cycle only)
  - single visit within a cycle
  - ❖ Multiple projects in one single proposal
  - ❖ Beam line has to schedule beam time with user

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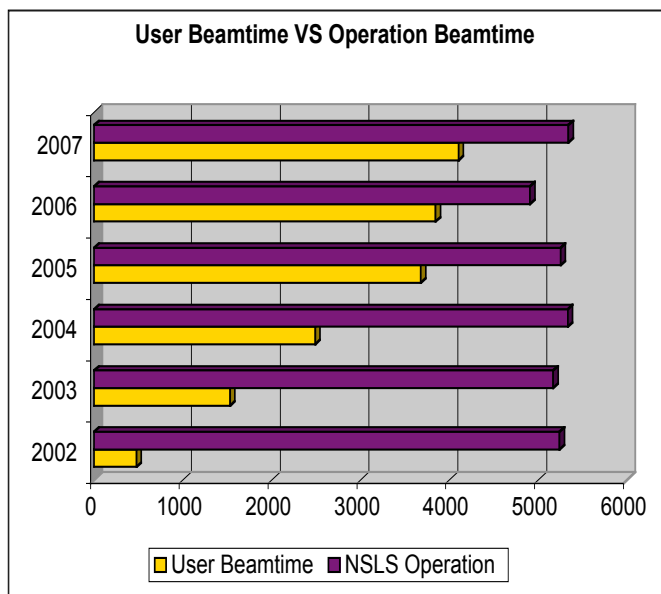
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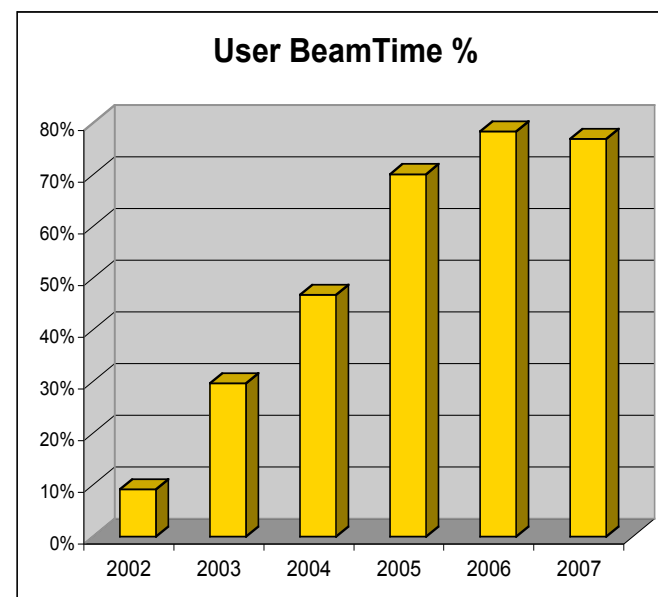
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# Available beam time



User scheduled beam time still increasing but reaching saturation.

The beam line continues to be oversubscribed as 102% of the beam time available to users has been scheduled in 2007.



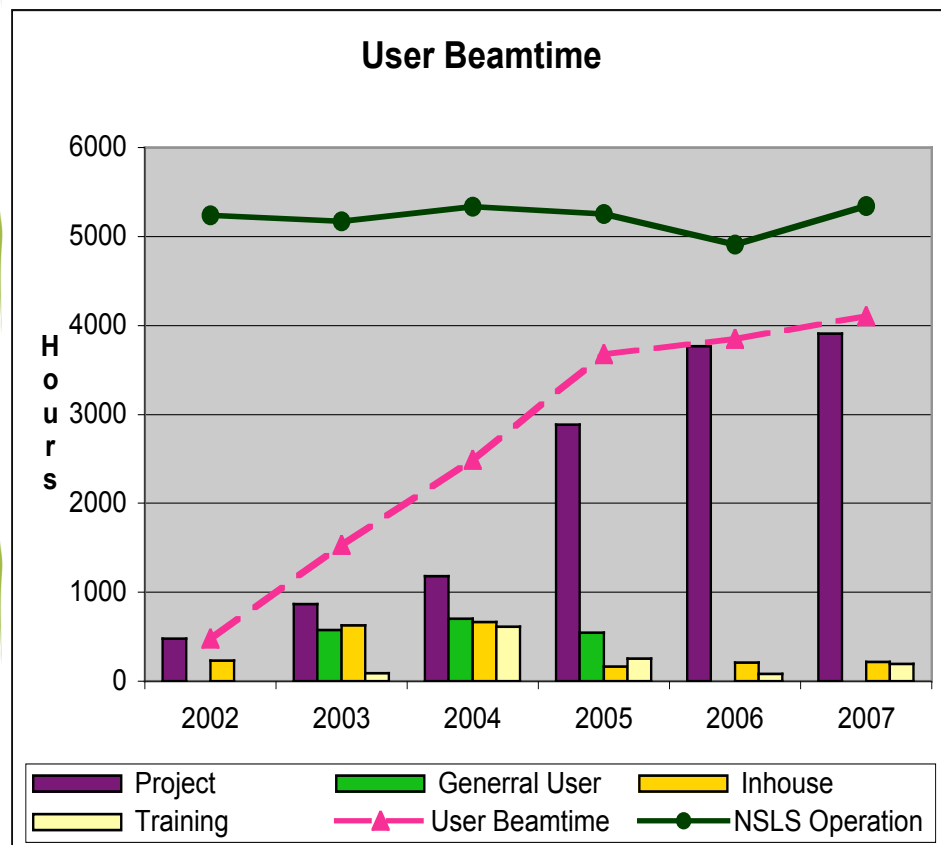


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# User beam time



## X6A operation

- X6A user projects 77%
- X6A beam line 17%
  - ✓ X6A commissioning 68%
  - ✓ X6A inhouse projects 32%
- Unused 10%

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## On site users

Most of the X6A projects are carried out by users who visit the facility

- Groups are in average composed of two individuals
- Average schedules are 1.5 days
- Mostly leave with image files and scaled data
- Some also leave with an electron density map

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## Automounter usage

- 10 groups requested the use of the automounter
- ~ 893 samples were screened
- ~ 50 data sets collected

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# Virtual users

## Virtual Users

- Not present during the measurement
- Send in their samples
- Receive image files and scaled data
- Usually also receive an electron density map

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Are required to have visited at least once

- 16 groups; Some were automounter users!

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# Remote users: exploring a new type of user

## Remote Users

- Not physically present at the facility
- Controls the experiment either assisted by local staff (Video Conferencing) or NoMachine technology with limited staff assistance

## Current status: commissioning

- Need the installation and development of sensors

“Educational” Movie can be downloaded from our web site!

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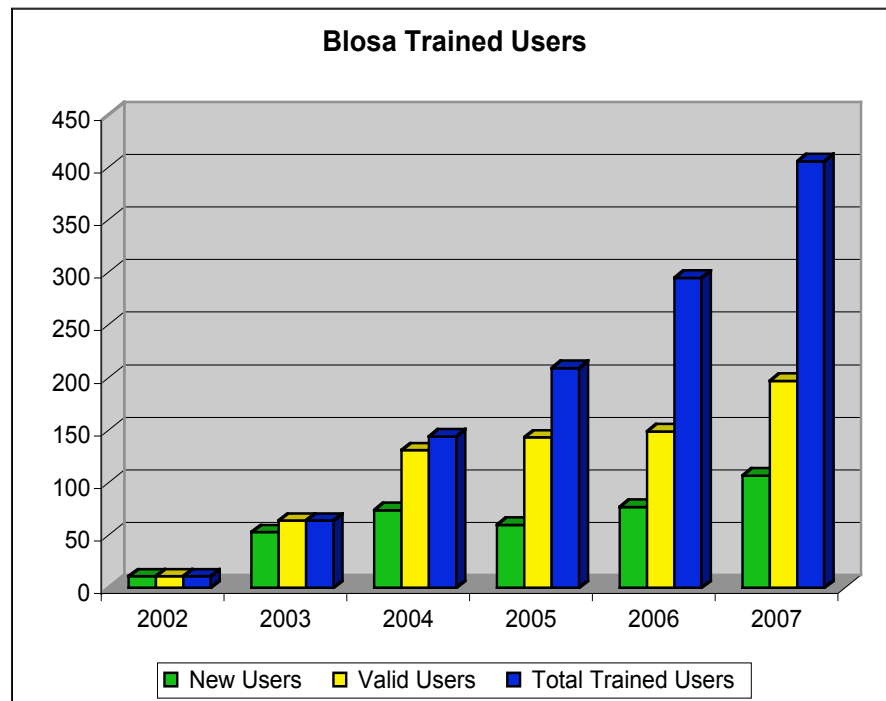
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## BLOSA (Beam Line Operation and Safety Awareness) trained users



BLOSA training is valid for two years.

\**New Users*: are experimenters who got trained in a specific year and were never BLOSA trained in previous years.

\**Valid Users*: are experimenters who keep a valid BLOSA Training Status in a specific year.

\**Total Trained Users*: are experimenters who trained in that year or before (accumulated number). Numbers include new and returning users.

In the past calendar year 107 new users were welcomed at the beam line; with 197 showing active user status.



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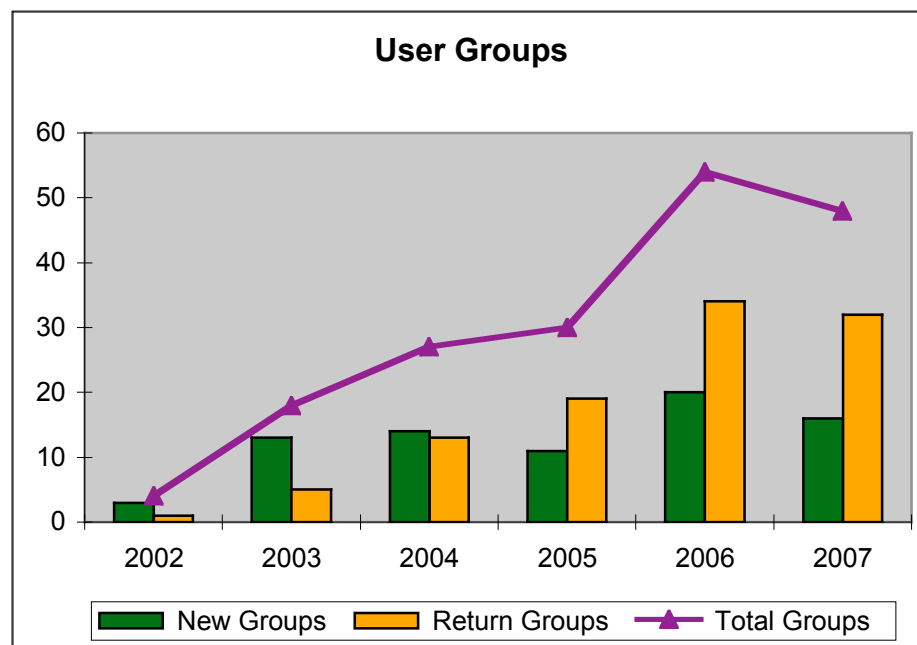
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# Consolidation of the user community\*



The number of user groups returning to the beam line is leveling off with 32 returning groups and 16 new user groups.

\*Source X6A Survey December 2007



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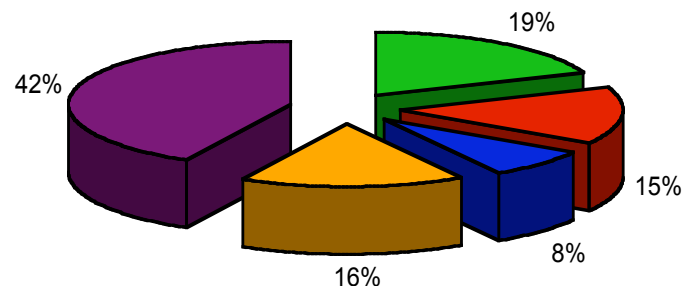
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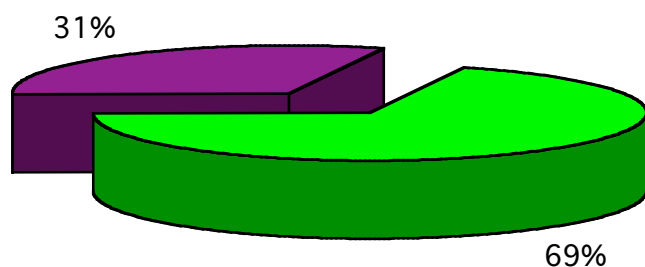
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## User demographics

58% of all user groups come from academic institutions located in the northeast region of the US.



■ International ■ Other US ■ Mid\_Atlantic ■ NY City ■ North East



■ Crystallographers ■ Non-Crystallographers

Expert and Non-Expert user groups. Only 60% of the users answered this line item in the survey.



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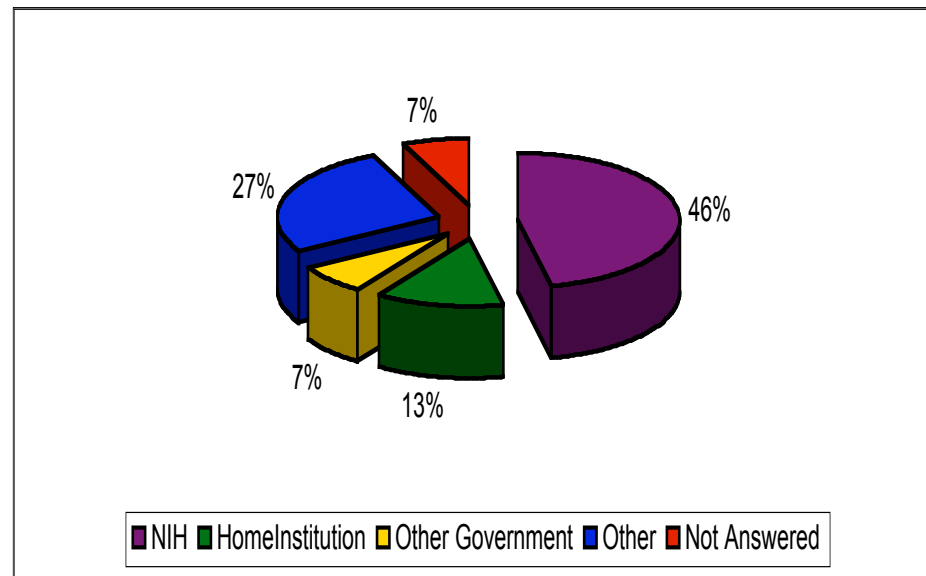
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# User Funding Sources



In relation to last year the number of groups supported by the NIH increased 1% and by home institutions 2%, while funding by other sources decreased. This is in direct relation to the X6A user base formed predominantly by researchers at the beginning of their careers.





# Impact



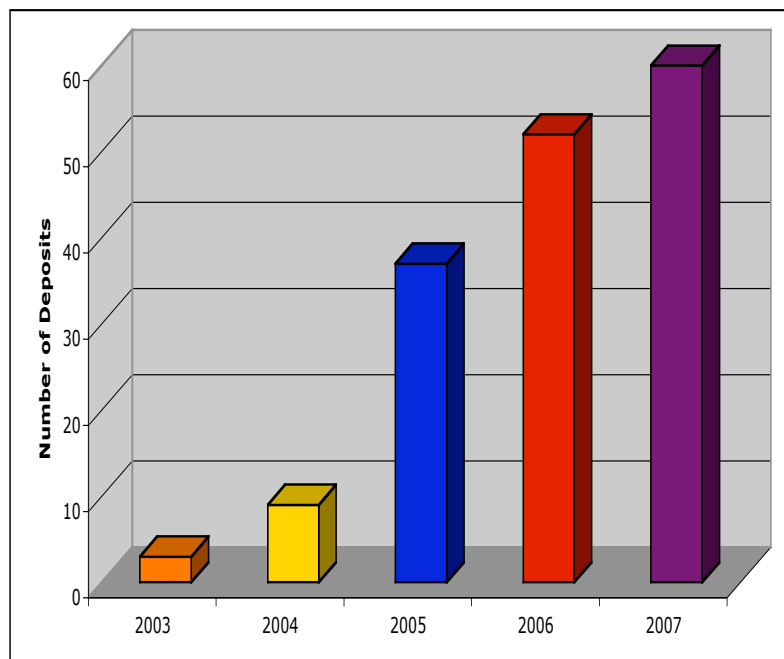
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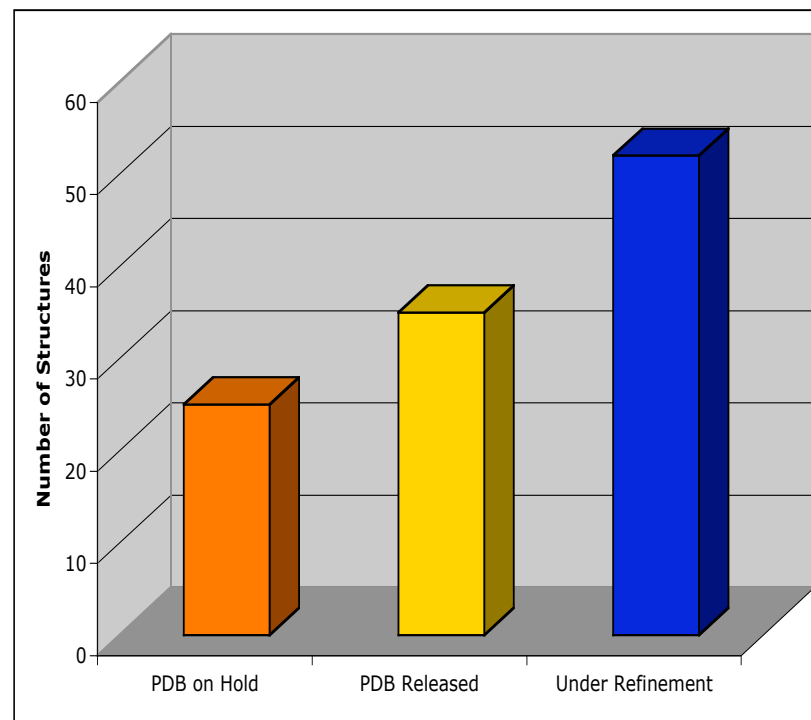
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# Protein Data Bank Deposits\*



Although the number of structures under refinement has decreased relative to 2006 it is still significantly larger than the structures released or on hold in 2007. It takes an average of 18 months for users to submit a PDB.

Number of deposits (released and on hold) continues to increase as the beam line matures.



\*Source X6A Survey December 2007



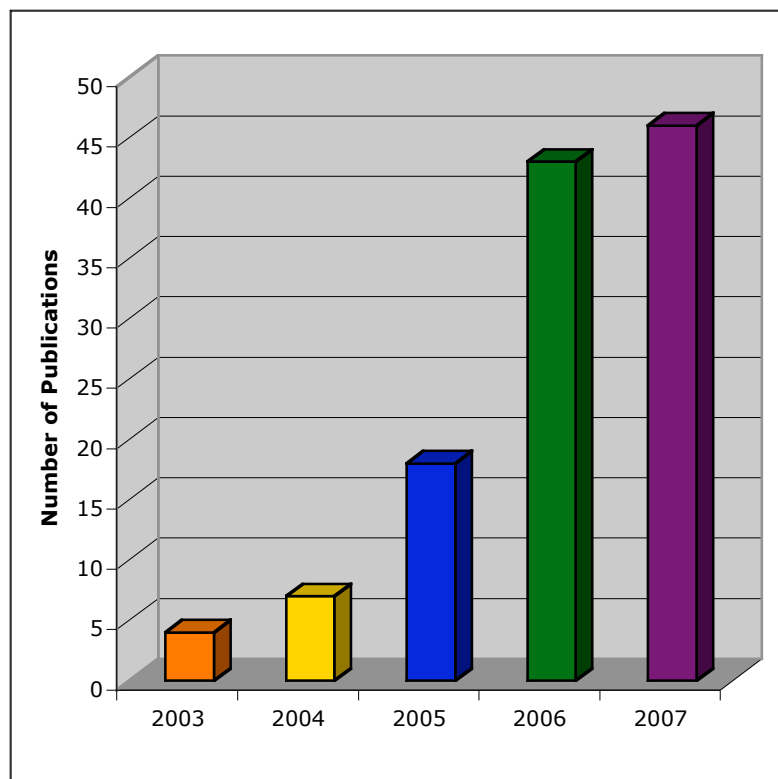
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## Publications\*



Publications*	
Total	High Impact**
118	55
2007	
46	21

\*Source X6A Survey December 2007

\*\* Journals with an impact of 6.0 or greater. Source JCR 2003

The total number of publications is leveling off indication of a mature beam line. Numbers are in direct relation to the X6A user community; young scientists establishing themselves. In spite of a thorough survey the total number of publications in a given year are not completely captured.



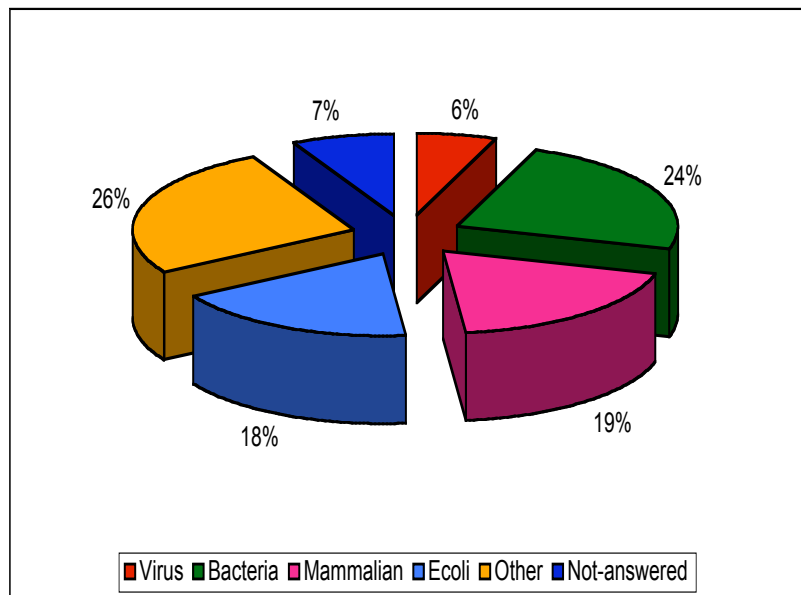
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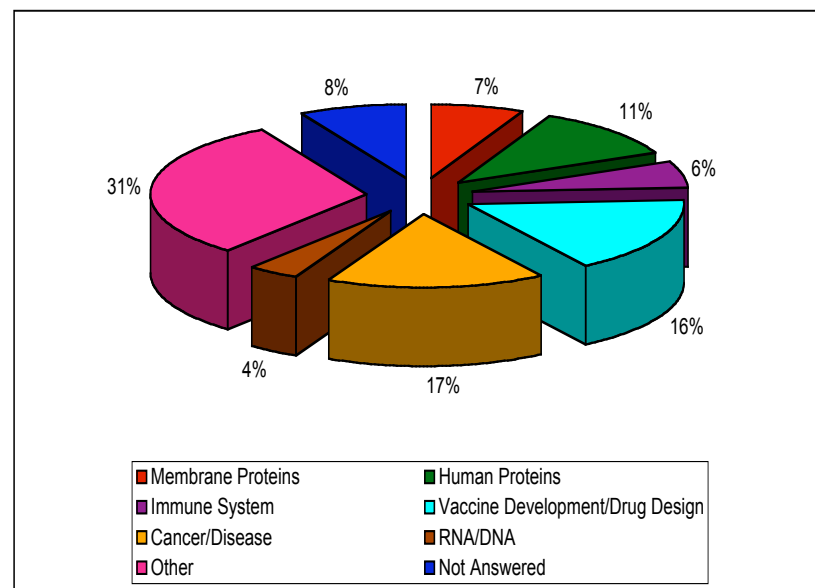
# Other impact factors\*

## Projects by Source organism



## Projects by Subject Area

61% of the projects developed at the facility focus on topics considered particularly challenging by the NIGMS\*\*; with an increase in the number of projects studying cancer and immune system related proteins



\*Source X6A Survey December 2007

\*\*Source NIGMS FY2006 and 2007 Budget

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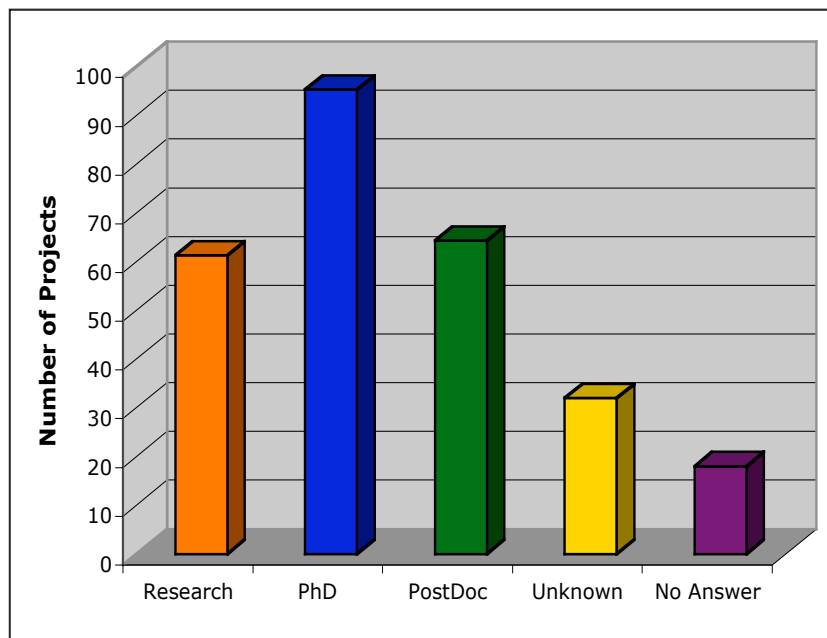
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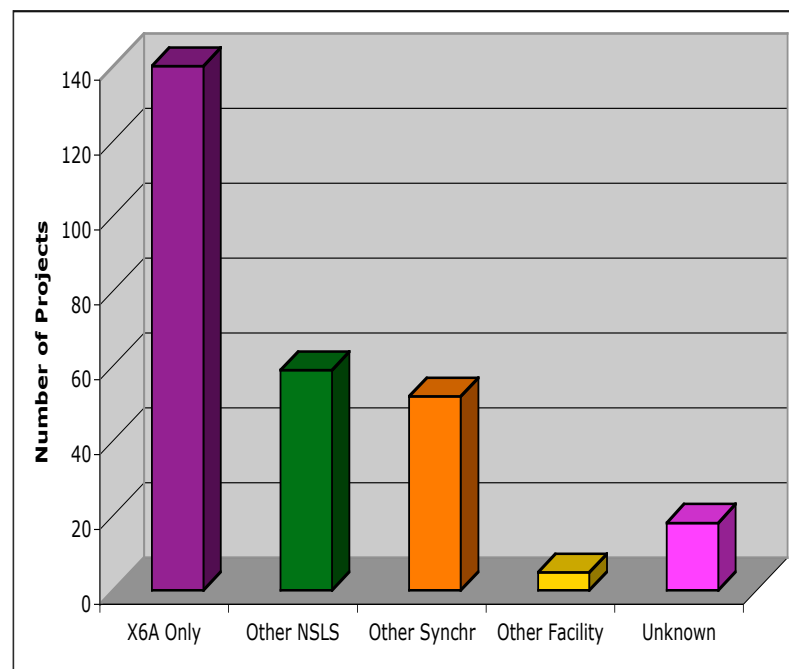
## Other impact factors\*



The number of projects carried out solely at the Facility increased by 13% over last calendar year, with 48% of projects also using other facilities. 6.5% did not answer to this line item in the survey.

\*Source X6A Survey December 2007  
25Feb2008

60% of projects developed at the facility support the training of a scientific workforce as reflected by the numbers of PhD and Post-Doctoral research projects; a 10 % decrease compared to last calendar year.



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# Synergy





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## Synergy

This year X6A users were able to benefit from the use of other beam lines and methods. Examples are:

- ❖ Small angle X-ray diffraction (Facility beam line, X21)
- ❖ X-ray absorption beam line

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X6A Facilities were also available to other NSLS Users and Students. Examples are:

- ❖ Infrared beam line (Facility beam line, U2A)
- ❖ Infrared beam line and circular dichroism (Facility beam line, IR 10B, Biology PRT U9B )

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# Synergy

*With other MX groups at the NSLS*

## ❖ X4 PRT

- User beam time re-allocation
- Technical and scientific approaches to crystallography
- Educational outreach

## ❖ PXRR

- X6A users in need of insertion device beam time has been allocated beam time on X29 during their X6A beam time
- Rapid Access

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# Synergy

The beam line has participated in the NSLS and BNL Education and Outreach programs

## *Education*

- Workshops and courses:
  - ❖ The X6A Workbench: Advanced Structural Biology Tools
  - ❖ Crystallization: focus on....
- BNL/Stony Brook Programs Office of Education:
  - ❖ SULI
  - ❖ Batelle

## *Outreach*

- ❖ Summer Sundays
- ❖ NSLS tours

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One participant of the “Crystallization: focus on ..... “ commented on the course survey: "I'm taking with me several things: First, an incredible and enriching experience; it was excellent to interact with people interested in the same things that I am, to learn from them, and to share information. I'm taking home a lot of ideas that I want to immediately put into action, I can't wait to do it."

About the X6A workbench:

“This is the best learning experience I’ve had from start to finish. .... We were able to go from the crystal to the structure. .... and because there were so few people here, everyone had a chance to do something.” KJ (2007)







# FUTURE

*Holds a fully automated crystal screening process*





## Short term goals: technical upgrades

- Diffractometer upgrade
  - ❖ Rotation axis
  - ❖ Slit assembly with ion chamber
  - ❖ Beam stop assembly
- Detector upgrade
- Computer workstations





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## Short term goals: technical development

- Improvement of the diffractometer upstream slit assembly:
  - ❖ Secondary slit box and Helium path
  - ❖ Inclusion of beam position monitor
  
- Automounter:
  - ❖ Integrate CrysCent and CrysIs as protocols for automated sample screening
  - ❖ Sample detection on goniometer head and inside gripper





## Short Term Goals: User program

### ➤ Beam Time Access:

- ❖ Provide a user friendly environment as many experimenters are first time synchrotron users;
- ❖ Consolidation of *Virtual User*, staff assisted sample automounter use;
- ❖ Develop reliable remote access





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## Summary

- Main focus of the operation IS the USER.
- Strong research program with good alignment with NIGMS mission.
- Young Faculty User base.
- Upgrade of Internet Services facilitates User access to beam time and facility management.
- Continued upgrade of instrumentation assures optimal beam time usage.
- Increased beam line productivity.
- Synergy with other methods and NSLS activities.

NSLS  
NIGMS





## The X6A Team

Marc Allaire  
Jean Jakoncic  
Kun Qian  
Vivian Stojanoff

*aaahhhh...personal attention! I love it!*  
*CM*